The Effect Of Ivy Gourd (Coccinia Cordifolia) Extract On Diabetic Patients
Anura V Kurpad and Rebecca Raj

The various factors that have contributed to the rise in the prevalence of diabetes in India include definite changes in eating habits and lifestyles that are increasingly sedentary and probable genetic factors that determine body fat distribution. Appropriate interventions in the form of weight reduction, changes in dietary habits and increased physical activity could help in preventing or delaying the onset of diabetes in India. Traditional health care systems which are widespread in developing countries, and the care of diabetics has been influenced by a growing interest in complementary and alternative medicine. Plants or their extracts may have a potential therapeutic role in the treatment for diabetes. Indian herbs such as Momordica charantia, Pterocarpus marsupium, and Trigonella foenum greacum have been reported to have hypoglycemic effect in type 2 diabetes, through stimulating or regenerating effects on beta cells, or through extrapancreatic effects. Coccinia indica, a plant that belongs to the Cucurbitaceae family and grows abundantly in India, has been widely used in the traditional treatment of diabetes mellitus. Studies have shown that the plant has an antidiabetic effect on alloxan-induced diabetic rabbits, in which a 95 per cent alcohol extract of the leaves at doses of 2.5 g/kg and 5.0 g/kg decreased blood glucose levels by approximately 50 per cent after six hours. Oral administration of 200 mg/kg of an aqueous ethanolic extract of the Coccinia leaf and fruits for 45 days to diabetic animals demonstrated a significant reduction in blood glucose, glycosylated hemoglobin (HbA1c) and increase in total hemoglobin and plasma insulin, suggesting that the administration of coccinia leaves to diabetic animals normalizes blood glucose. While literature on the potential efficacy of Coccinia indica in the treatment of human diabetes does exist, it is relatively sparse and heterogenous. Freeze dried Coccinia indica leaves, when administered orally twice a day for six weeks to patients with untreated but uncomplicated maturity onset diabetes, demonstrated hypoglycemic activity with significant improvement in glucose tolerance. However, many details about the exact dose administered, or patient characteristics, for example, if the body weight or food intake of the patients changed during the course of the treatment were not clear in this earlier study, and certainly suggested the need for further studies. Therefore, the aim of the present study was to carefully evaluate the effectiveness of an aqueous alcoholic extract of Coccinia cordifolia, in a dose of 1 g/d (equivalent to 15 g of the dried plant, or 50 gm of wet weight), on the blood glucose levels of newly detected type 2 diabetic patients requiring only dietary or lifestyle treatment.

Methods

The study was a double blind, placebo controlled, randomized trial. Sixty newly detected type 2 diabetic patients (33 male and 26 female subjects, aged between 35 and 60 years) needing only dietary or lifestyle modifications (with fasting blood glucose in the range of 11 0 – 180 mg/dl) were recruited into the study. One subject dropped out of the study and 59 subjects completed the study; there were 30 subjects in the placebo group and 29 subjects in the experimental group. Exclusion criteria were the presence of any chronic disease and the concurrent use of any medication for the control of blood sugar levels. After recruitment, the subjects were randomly assigned into the placebo or experimental group. The study was approved by the institutional ethical review committee of St. John’s Medical College and informed consent was obtained from the subjects.

The aerial parts of Coccinia cordifolia, including the leaves and fruits (in a ratio of 30:70 respectively) were extracted with aqueous alcohol. The extraction was with 50 per cent alcohol (1:1 alcohol and water), and the extract was purified and filtered. The clear filtrate was spray dried. Fifty gm of the wet weight of leaves and fruit (15 gm of the dry weight) yielded 1 gm of the extract. Maltodextrin capsules (500 mg) were used as placebo, and both capsules were prepared by Green Chem, Bangalore, India. Prior to the intervention, the subjects underwent...
baseline investigations which included anthropometric, biochemical, dietary and physical activity assessment. The extract was administered as two 500 mg capsules daily (1 gm/day) for 90 days, during which the subjects reported weekly to the Nutrition Clinic to record their body weight, collect their weekly capsule supply and report adverse events, if any. The compliance of the subjects to the ingestion of capsules was documented every week when they reported to the Nutrition Clinic. The subjects were provided with a capsule calendar in which they were required to tick mark boxes relating to the daily intake of capsules and also to note down any missed capsule. All the study subjects were provided with standard dietary and physical activity advice for the control of their blood sugars. In case of overweight patients, advice was provided to achieve moderate weight loss of about 5 per cent over the study duration. The standard advice also included regular physical activity, with dietary strategies to increase dietary fiber (legume, fruits and vegetables) and decrease intake of fat.

Anthropometric measurements were standardized and included body weight, height, skinfold thickness and mid-arm, waist and hip circumferences. Skinfold measurements in triplicates were carried out using Holtain skinfold calipers, at four sites (i.e.) biceps, triceps, subscapular and suprailiac. The average sum of four skinfold measurements were used to compute body density using the age and gender specific equation and percent body fat was derived from body density. These equations were previously validated in a group of Indian men and women. The measurements were taken at baseline and repeated at day 45 and day 90 of the intervention period.

Fasting and post prandial blood glucose, glycosylated hemoglobin and lipid profile were measured at baseline, day 45 and day 90 of the study period. The blood glucose, triglyceride, total and High Density Lipoprotein (HDL) cholesterol were estimated by spectrophotometric assays on automated clinical chemistry analyzer - Dimension RxL (Dade Behring, Newark, USA). All assays were calibrated by use of Dade Dimension human calibrator (Dade Behring Inc, Newark, USA). The analytical coefficient of variation (inter-assay) for total cholesterol, triglycerides and HDL cholesterol were 4.1 per cent, 4.7 per cent and 4.1 per cent respectively, while it was 2.6 per cent for glucose and 3.2 per cent for HbA1c.

Dietary assessment was carried out using a 24 hr recall at baseline, and repeated at day 45 and day 90 of the intervention period. The data from the dietary recall was used to arrive at estimates of daily nutrient intake from standard recipes, using the published food composition databases. The routine physical activity pattern of the subjects was assessed using a questionnaire carried out at baseline, day 45 and day 90 of study period.

The data are presented as Mean ± SD. An independent 't' test analysis was performed to ascertain whether significant differences existed between the anthropometric and biochemical parameters of the subjects in the experimental and placebo group at baseline. A repeated measure ANOVA with group as a factor was performed to assess the change over time in the anthropometric, biochemical and food intake parameters between the two groups. The repeated measure ANOVA was then used to assess for significant differences between the various time points.

<table>
<thead>
<tr>
<th>Table 1: Profile of subjects at baseline</th>
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<tbody>
<tr>
<td><strong>Group</strong></td>
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<tr>
<td>Age (yrs)</td>
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<tr>
<td>Body weight (kg)</td>
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<tr>
<td>Per cent Body Fat #</td>
</tr>
<tr>
<td>Hemoglobin (g %)</td>
</tr>
<tr>
<td>Glycosylated Hb (HbA1c) (%)</td>
</tr>
<tr>
<td>Fasting blood glucose (mg/dl)</td>
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<tr>
<td>Post prandial blood glucose (mg/dl)</td>
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<tr>
<td>Total cholesterol (mg/dl)</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
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<tr>
<td>LDL cholesterol (mg/dl)</td>
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<tr>
<td>TG (mg/dl)</td>
</tr>
</tbody>
</table>

Mean ± Standard deviation (SD)

# - Calculated from the sum of four skinfold measurements and applying the formulæ of Durnin and Womersley (1974)

No significant differences were observed in any of the parameters of the subjects of the two groups (Independent 't' test)
At the end of the study period, no groups (repeated measure ANOVA). Body fat over time between the two groups (repeated measure ANOVA). No significant differences observed in the change of hemoglobin, total cholesterol, LDL cholesterol and serum triglycerides over time between the two groups (repeated measure ANOVA). The LDL cholesterol of the experimental group was significantly lower (14.6 per cent) at day 90 when compared to the initial values (repeated measures ANOVA).

There was no significant change in daily energy intake of the subjects (n = 59) from 1740.5 ± 500.4 kcals at baseline and 1679.7 ± 516.8 kcals at day 90. The protein, fat and carbohydrate intake of the subjects also did not show any significant change. When these data were analyzed between groups, there was also no significant difference. Additionally, the body weight and body mass index of the subjects did not change significantly at the end of the study.

The mean reported compliance of the subjects in the experimental group to their prescribed diet was 93 per cent (65-100 per cent) and 88 per cent (38-100 per cent) to prescribed physical activity, while in the placebo group it was 94 per cent (50-100 per cent) to prescribed diet and 84 per cent (16.7-100 per cent) to prescribed physical activity. The physical activity pattern of both the experimental and placebo group did not change during the study.

There were no serious adverse events reported by the subjects of the present study. The observed adverse events were minor and limited to initial mild symptoms of the gastrointestinal tract such as abdominal distention, flatulence, constipation and gastritis in a few subjects. These symptoms subsided within a week in all subjects.

Discussion

Approaches to the control of and prevention of hyperglycemia are central to the management of diabetes mellitus. While drugs, diet and physical activity are the cornerstone for the treatment of diabetes, there is growing interest in complementary and alternative medicine for diabetes, not only among general public but also among health care providers, researchers, educators. Plant remedies may be appealing as an alternative and adjunctive treatment for diabetes.
Even though all the subjects of the present study were provided standard dietary and physical activity advice, there was no significant change in daily energy intake and body mass index of the subjects. It is possible that the prescribed dietary and physical activity advice was either not followed, or not completely initiated by the subjects, even though the self-rated compliance to the dietary and physical activity advice was greater than 80 per cent in both the groups. Therefore, the results of the present study suggest that the decrease in fasting (16 per cent) and post prandial blood (18 per cent) glucose observed in experimental group could be attributed to the hypoglycemic effect of the coccinia cordifolia extract.

Coccinia indica (ivy gourd) is a creeper that grows widely in India and Bangladesh. The plant has been used since ancient times as an antidiabetic drug by physicians who practice Ayurveda. A double blind control trial (n = 32) conducted in India, demonstrated significant improvement in glycemic control following 6 weeks use of powder from locally obtained crushed dried leaves of Coccinia indica in poorly controlled or otherwise untreated patients with type 2 diabetes, however there was no data available to indicate if the body weight changed. In another three arm, controlled clinical trial (n = 70), the use of dried herb pellets made from fresh leaves of Coccinia indica was compared with no treatment and oral hypoglycemic agents (chlorpropamide). The improvement in glycemic control observed in the group that was treated with the herb was similar to that with a conventional drug. However, no details were available on whether the body weight or food intake of the patients changed during the study period. Additional studies have also provided supporting evidence for the hypoglycemic effect of Coccinia indica. Yeh et al., 2003, while assessing the quality of the evidence of herb for glycemic control, employed the American Diabetes Association Criteria for Clinical Guidelines and rated Coccinia indica with A rating, having supportive evidence with at least one adequate randomized clinical trial. In the present study, the dose of the aqueous alcoholic extract of Coccinia indica was higher than in the previous two human studies, in which 2-6 g/d of the dried leaves were administered. The higher dose in the present study (1 g of the aqueous alcoholic extract was equivalent to 15 g of the dried herb) was chosen since personal discussions with local ayurvedic practitioners revealed that they empirically used ‘a handful’ of the dried herb (equivalent to 15 g) daily in their treatments. In addition, they also reported absolutely no adverse events, which was also reflected in the published studies albeit at lower doses. In the present study, very minor side effects were reported, which could not be attributed specifically to the herb. In addition, it should be emphasized that the findings from this study cannot automatically be translated into the eating of the cooked plant. While the extract was heat stable, it was extracted from the dried aerial parts of the plant, and not

### Table 3: Biochemical parameters of the subjects at baseline, Day 45 and Day 90 of the study

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Day 45</th>
<th>Day 90</th>
<th>P value</th>
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<tbody>
<tr>
<td><strong>Glycosylated Hb (HbA1c) (%)</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Placebo</td>
<td>6.4 ± 0.9</td>
<td>–</td>
<td>6.3 ± 0.9</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Experimental</td>
<td>6.7 ± 1.2</td>
<td>–</td>
<td>6.1 ± 1.1b</td>
<td></td>
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<tr>
<td><strong>Total cholesterol (mg/dl)</strong></td>
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<tr>
<td>Placebo</td>
<td>203.6 ± 46.2</td>
<td>191.8 ± 33.1</td>
<td>187.3 ± 37.9</td>
<td>0.72</td>
</tr>
<tr>
<td>Experimental</td>
<td>207.1 ± 64.6</td>
<td>202.2 ± 38.5</td>
<td>191.3 ± 41.8</td>
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<tr>
<td><strong>HDL cholesterol (mg/dl)</strong></td>
<td></td>
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<tr>
<td>Placebo</td>
<td>39.7 ± 10.0</td>
<td>40.6 ± 7.2</td>
<td>38.8 ± 8.3</td>
<td>0.72</td>
</tr>
<tr>
<td>Experimental</td>
<td>44.7 ± 13.4</td>
<td>45.2 ± 13.3</td>
<td>44.9 ± 12.3</td>
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<tr>
<td><strong>LDL cholesterol (mg/dl)</strong></td>
<td></td>
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<tr>
<td>Placebo</td>
<td>138.3 ± 48.8</td>
<td>128.4 ± 32.8</td>
<td>133.9 ± 36.2</td>
<td>0.18</td>
</tr>
<tr>
<td>Experimental</td>
<td>141.8 ± 50.3</td>
<td>131.2 ± 30.9</td>
<td>121.1 ± 26.4</td>
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<tr>
<td><strong>Serum Triglycerides (mg/dl)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Placebo</td>
<td>185.0 ± 74.6</td>
<td>158.9 ± 61.7</td>
<td>173.1 ± 87.3</td>
<td>0.36</td>
</tr>
<tr>
<td>Experimental</td>
<td>184.0 ± 131.3</td>
<td>177.3 ± 68.9</td>
<td>162.2 ± 92.0</td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD
n= 30 in placebo & n = 29 in experimental group
+ significant difference between time points within each group (repeated measure ANOVA)
a- measured only at 2 time points (baseline and day 90) and paired 't' analysis was performed
b- significant difference between baseline and day 90.

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**Legend:**
- Solid lines: Experimental group; Dashed lines: Control Group.
- Solid circles or squares = experimental group.
- Open circle or squares = Control group.
- Circles (solid or open) = post-prandial glucose levels; Squares (solid or open) = Fasting Glucose levels.
- *- P<0.01; significant interaction between time points and group (repeated measure ANOVA with group as between subjects factor).
from the cooked vegetable. It might, therefore, be prudent to assume that the active principle would not survive a great deal of cooking.

The mechanism of action of Coccinia indica is not well understood, but the herb appears to be insulin mimetic. The oral administration of pectin isolated from Coccinia indica fruit showed a significant hypoglycemia effect in normal rats. It has been postulated that the ingredients present in the extract of Coccinia indica such as triterpenes, act like insulin, correcting the elevated enzymes Glucose-6-phosphatase, lactase dehydrogenase (LDH) in glycolytic pathway and restore the LPL activity in lipolytic pathway with the control of hyperglycemia in diabetes. When coccinia indica and momordica charantia extracts were administered to diabetic rats, the results indicated that there was lowering of blood glucose by depressing its synthesis through depression of the key gluconeogenic enzymes glucose-6-phosphatase and fructose-6-biphosphatase and also by enhancing glucose oxidation by the shunt pathway through activation of its principal enzyme G6PDH.

The results of the present study suggest that Coccinia cordifolia (synonym Coccinia indica) has a potential hypoglycemic action independent of energy/food intake or weight loss and thus could represent a possible dietary adjunct for the treatment of diabetes in patients with mild diabetes. Future studies are needed to more precisely define targeted populations with regard to disease classification, severity, and optimal adjunctive interventions. It will also be important to elucidate mechanisms of action so that the applicability to type 1 or type 2 can be clarified.

Acknowledgements

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References

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**Annual Foundation Day**

The Annual Day of the Foundation was held on November 29, 2007. On this occasion Dr V Prakash, Director Central Food Technological Research Institute, Mysore delivered the C Ramachandran Memorial Lecture on “Food Technology for Better Nutrition”.

**Symposium on “Food Technology for Better Nutrition”**

Following the Foundation Day, NFI organized a two-day Symposium on Food Technology for Better Nutrition on November 30th and December 1st, 2007 at India International Centre, New Delhi.

Food being an essential requirement for survival, Man has been engaged in the quest for food ever since the dawn of creation and had used technology within his means for securing edible food. Food Technology, therefore, is as ancient as Mankind. With advances in Science and Technology and with changing needs induced by development, the scope for Food Technology has vastly increased. Advances in science have also opened up possibilities of Biofortification and Genetic Engineering, which could result in enhancing the nutritive value of foods.

The symposium had three major themes:

a. technology for improving nutrient content of crops through bio-fortification

b. technology for reducing wastage of vegetables and fruits and processing of millets, oils and vegetables and

c. food fortification to combat micronutrient deficiencies.

Peer reviewed online Journal “Comprehensive Reviews in Food Science and Food Safety” has agreed to review and publish the papers presented in this Symposium. A brief summary of the presentations is given in below:

**Biofortification:** Diets of poorer segments of population in most developing countries consist mostly of staples. Two presentations outlined the efforts to develop and distribute varieties of food staples, which are high in iron, zinc, and provitamin A. Studies undertaken in Africa showed that consumption of biofortified vitamin A rich sweet potato and maize resulted in improved vitamin A status of children. In India, Department of Biotechnology, has launched the Indian Biofortification Network Project, involving more than 15 research and development institutions, with an overall objective of developing suitable genotypes with increased iron and zinc content in Rice, Wheat and Maize.

Technology for processing of millets, oil, vegetables and fruits: Millets rich in micronutrients were a part of Indian diets. Many speakers dwelt on the technologies for improved production of millets; others emphasized the use of technologies such as blanching, acid treatment, malting, fermenting, dry heating and popping for processing of millets such as sorghum and pearl millet to reduce anti-nutritional factors and increase the digestibility and shelf life. Malaysian Palm Oil Board has developed and patented technology for processing palm oil which preserves phytonutrients in palm oil; the potential beneficial effects of use of this oil was discussed.

India currently ranks as number one in the world in the production of vegetables and number two in the production of fruits but per capita consumption of vegetables in India is quite low. India aims at 4 percent growth in agriculture and this is possible only with high growth in horticultural sector backed with appropriate investment in processing, storage and transport of fruits and vegetables so that farmers get appropriate returns for horticultural investment, and people get access to vegetables at affordable cost so that they consume adequate vegetables. Village-based and cottage-based food technology for processing vegetables can contribute to income generation and poverty reduction. Special reference was made to low cost technologies for turning waste into useful product by highlighting a specific example of Integrated Post Harvest Management of cauliflower. Speakers emphasized that as there is growing awareness about importance of eating vegetables and fruits, improved access to vegetables including good quality processed vegetables right through the year at affordable cost can result in substantial increase vegetable consumption in home diets of middle income groups, especially, in urban areas.

**Food fortification:** Technologies for food fortification of some of the commonly consumed food items have been developed and they are widely used for improving the micronutrient intake, especially, among poorer segments of the population in many countries. In India fortification of salt with iodine is mandatory and use of non-iodised salt for human consumption has been banned. Inspite of this, nearly half the households in India consume non-iodised salt and incur the risk of Iodine Deficiency Disorders. Studies from Sikkim have shown that the incidence of endemic cretinism and goiter was nearly eliminated within a decade through improved access to iodised salt. Iron deficiency and anaemia affect majority of Indians. Fortification of salt with iron has been shown to be one of the most effective, economical and sustainable methods for improving iron intake among poorer segments of our population. Data on research efforts of the National Institute of Nutrition for development of technology for iron and iodine fortification of salt and assessment of impact of use of the double fortified salt on iodine and iron status of the population was discussed.

Experiences on the use of food fortification for combating micronutrient deficiencies in Thailand were presented and discussed. World Food Programme is supplying processed food such as India mix fortified with minerals and vitamins to Integrated Child Development Services; there are ongoing studies on wheat flour fortification in Gujarat, development of new types of ready-to-use-foods and fortified food for people suffering from HIV/AIDS.

**Study Circle Lectures**

“Child Nutrition: Current Concerns” by Dr Shanti Ghosh (Consultant, Mother and Child Health) on 31st October 2007.

“Oils and Fats - Characteristics and Sensory Attributes” by Dr Pushpa Sundararaj (Reader, Department of Food and Nutrition, Lady Irwin College, University of Delhi) on 28th December 2007.